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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,380	02/24/2004	Mary Jane Cardosa	2316.2009-000	3579
22852	7590	08/17/2007		
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP 901 NEW YORK AVENUE, NW WASHINGTON, DC 20001-4413			EXAMINER CHEN, STACY BROWN	
			ART UNIT 1648	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/786,380	Applicant(s) CARDOSA ET AL.	
	Examiner Stacy B. Chen	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 35-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 35-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>5/31/07; 6/20/07</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's response and amendment filed June 20, 2007 is acknowledged and entered. Claims 1 and 35-46 are pending and under examination. In view of the new grounds of rejection this Office action is made non-final.

Response to Amendment/Arguments

2. The following objections and rejections are withdrawn:
 - The objection to the specification is withdrawn in view of Applicant's amendment to the specification, updating the status of related application USSN 09/147,919, now U.S. Patent 6,869,793.
 - The objection to claim 1 and dependent claims 35-46 for reciting improper grammar is withdrawn in view of Applicant's amendment.
 - The rejection of claim 37 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of Applicant's amendment.
 - The rejection of claims 1 and 35-46 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent 6,869,793, is overcome by the filing of a terminal disclaimer.

Claims Summary and Interpretation

3. The claims are drawn to a recombinant modified vaccinia virus Ankara (MVA) comprising a DNA sequence encoding a dengue virus antigenic epitope of serotype 1, 2, 3 or 4.

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The Office understands that the DNA sequence encodes an antigen comprising an epitope, since epitopes can be conformational (structure is dependent on surrounding amino acids that are not part of the epitope itself). In another embodiment, the DNA sequence encodes a preM antigen, E antigen, or NS1 antigen of dengue virus, wherein each antigen comprises an epitope.

Specifically, the DNA sequence is inserted into the MVA at the site of a naturally occurring deletion, such as deletion site II. The DNA sequence is under transcriptional control of the vaccinia virus early/late promoter P7.5. Also claimed is a composition comprising the recombinant MVA and a pharmaceutically acceptable carrier or diluent. The composition is used to generate an immune response in an animal, such as a human, upon administration. Also claimed is a cell, a eukaryotic cell, comprising the recombinant MVA. The cell is used to produce recombinant MVA when cultured under suitable conditions and subsequently isolated.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 37 and 41-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Sutter *et al.* (*Developments in Biological Standardization*, 1995, 84:195-200, "Sutter") in view of Lai *et al.* (US 5,494,671, "Lai"). The claims are summarized above. Sutter teaches that MVA is a useful vaccinia vector for live recombinant vaccines, having the advantage of lower virulence in humans (see entire document). Sutter discloses that MVA constructs expressed antigens of interest in chicken embryo fibroblasts (eukaryotic cells), see page 198, second paragraph. Sutter does not suggest that Dengue DNA be expressed in the recombinant viral construct. However, Lai teaches a vaccine comprising Dengue DNA in a vaccinia vector, see for example claims 1 and 2. It would have been within the ability of one of ordinary skill in the art to combine the Dengue DNA, as taught by Lai, with the MVA vector as taught by Sutter, for the purpose of producing a Dengue vaccine with a less virulent vaccinia vector, as taught by Sutter. Other advantages include the ability to support high titers of protein production in chicken embryo fibroblasts, restricted host range, avirulence in animals, extensive safety testing humans, late-stage block in non-permissive cells, high-level recombinant gene expression, and high immunogenicity as a recombinant vaccine (page 199, second paragraph). One would have had a reasonable expectation of success that the MVA vector would have been able to express the Dengue DNA of Lai's vector because both MVA and Lai's vector are vaccinia. The advantage of using MVA, as taught by Sutter, is that MVA is less virulent in humans.

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6. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Sutter *et al.* (*Developments in Biological Standardization*, 1995, 84:195-200, "Sutter") in view of Lai *et al.* (US 5,494,671, "Lai"), as applied to claim 1 above, and further in view of Altenburger (US Patent 5,185,146). Claims 40 requires that the DNA sequence in the recombinant MVA be under the control of the vaccinia virus early/late promoter P7.5. Neither Sutter nor Lai disclose the use of the P7.5 promoter.

However, Altenburger discloses that recombinant vaccinia viruses derived from MVA that contain a DNA sequence encoding a foreign antigen are under the control of the transcriptional promoter, such as the 7.5 kDa gene (col. 3, lines 39-47). It would have been obvious to one of ordinary skill in the art to use regulatory sequences, such as transcriptional promoters for the expression of foreign DNA sequences. One would have been motivated to use the 7.5 promoter (P7.5) in Sutter's MVA construct because Altenburger suggests that the 7.5 promoter is useful in the MVA construct, or virus vectors derived from MVA, for expressing the heterologous DNA sequence of interest. Given Altenburger's suggestion to use a promoter, and the specific reference to P7.5, one would have been motivated to use the P7.5 promoter. Further, one would have had a reasonable expectation of success that the P7.5 promoter would have worked in Sutter's MVA construct because Altenburger teaches that the P7.5 promoter is useful in MVA constructs, or virus vectors derived from MVA.

7. Claims 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sutter *et al.* (*Developments in Biological Standardization*, 1995, 84:195-200, "Sutter") in view of Lai *et al.* (US 5,494,671, "Lai") as applied to claim 1 above, and further in view of Sutter *et al.* (*PNAS*

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89:10847-10851, 1992, "Sutter II"). Claims 38 and 39 require insertion of one or more sequences at the site of one or more naturally occurring deletions in the MVA genome. The teachings of Sutter and Lai are summarized above; neither teach or suggest insertion at the site of a naturally occurring deletion in the MVA genome.

Sutter II teaches insertion of a foreign sequence at the site of a naturally occurring deletion in MVA, and indicates that MVA has six major deletions totaling 31,000 base pairs (abstract and page 10847, first column, first paragraph after abstract). Therefore, given the known deletions (six major deletions), it would have been obvious to choose one or more of the naturally occurring deletion sites in MVA as a location for inserting one or more foreign DNAs, such as the dengue DNA.

8. Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sutter *et al.* (*Developments in Biological Standardization*, 1995, 84:195-200, "Sutter") in view of Lai *et al.* (US 5,494,671, "Lai") as applied to claim 1 above, and further in view of Moss (*Seminars in Immunology* 2:317-327, 1990) and Monath *et al.* (*Fields Virology*, 1996, Third Edition, Lippincott-Raven Publishers, Philadelphia, pages 961, 997-1000).

These claims differ from the above in requiring the recombinant MVA to contain DNA encoding antigens of all four serotypes of Dengue. Moss teaches that recombinant vaccinia vaccine vectors can be used as "polyvalent vaccines containing multiple genes from one microorganism or several", see page 322. Monath discloses that there are four dengue serotypes, and that it is possible to sustain multiple, sequential infections (page 999, second column, second paragraph). Therefore one of ordinary skill in the art would have had motivation to induce an

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immune response against all four dengue serotypes, and Moss provides motivation to place multiple genes in one virus. In view of the combined teachings of the references, one of ordinary skill in the art would have been motivated to further modify the recombinant virus by use of antigens of the four different serotypes, to provide cross-immunization against all forms of the dengue virus. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 35-37 and 41-46 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 36, 37, 39, 41-48, 50 and 79 of copending Application No. 10/497,633 (common inventor Mary Jane Cardosa). Although the conflicting claims are not identical, they are not patentably distinct from each other because

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the co-pending claims are drawn to an MVA vaccinia virus vector comprising DNA encoding Dengue virus NS1 protein, a species of the instantly claimed genus, drawn to a recombinant MVA containing and capable of expressing at least one DNA sequence encoding a Dengue virus epitope. A species anticipates a genus. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

10. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campbell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 8-13-2007
Primary Examiner, TC1600